REMARKS

Claims 25-29 are pending in the present case. The Examiner has rejected these Claims in an Office Action mailed June 2, 2004, and again in an Advisory Action mailed January 10, 2005, under 35 U.S.C. § 102(b) as allegedly being anticipated by Chen TT et al. (J. Immunology 1994; 153:4775-4787) (hereinafter "Chen").

1.   Claims 25-29 recite the expression of at least three *different* variable regions.

In the previously filed response, Applicant explained that Claims 25-29 recite the expression of at least 3 <u>different</u> variable regions (see, *e.g.*, Claim 25, part b) using nucleic acid isolated from malignant B-cells. In the Advisory Action of January 10, 2005, the Examiner asserts that the claims do not require expression of three variable regions. Applicant respectfully disagrees. The claims expressly require expression of at least three different variable regions. In particular, the three different variable regions are recited to comprise any of the following combinations:

1. one V_H region and at least two <u>different</u> V_L regions (a total of three <u>different</u> variable regions)

2. two <u>different</u> V_H regions and one V_L region, (a total of three different variable regions.

3. two <u>different</u> V_H regions and at least two <u>different</u> V_L regions (a total of four <u>different</u> variable regions.

The claims indicate that the recited "at least two V_L regions" are <u>different</u> V_L regions by requiring that they differ from each other by at least one idiotope. Similarly, claims indicate that the recited "at least two V_H regions" are <u>different</u> V_H regions by requiring that they differ from each other by at least one idiotope. See, e.g., part (b) in each of Claims 25, 28 and 29.

Thus, the claims in the present application each require expression of <u>at least 3</u> <u>different</u> variable regions to produce the claimed multivalent compositions.

2.   A single immunoglobulin does not provide at least three <u>different</u> variable

regions.

Whole immunoglobulins (*e.g.*, such as those expressed by normal B-cells) comprise two <u>identical</u> heavy chains and two <u>identical</u> light chains (see, *e.g.*, the National Cancer Institute web page http://press2.nci.nih.gov/sciencebehind/immune/immune10.htm, a printed copy of which is attached hereto). A single immunoglobulin, therefore, provides only *two* <u>different</u> variable regions - one from the heavy chains and one from the light chains. Because the V_H regions are identical to each other, the V_H regions of a single immunoglobulin do <u>not</u> differ by any idiotopes. Similarly, the V_L regions of a single immunoglobulin are identical to each other, and thus the V_L regions do <u>not</u> differ by any idiotopes. For this reason, a single immunoglobulin provides only <u>two</u> different variable regions, *not the three <u>different</u> variable regions required by the present claims.*

3.   Chen provides only two different variable regions

<u>A. Chen provides variable regions from a single immunoglobulin.</u>

As previously noted, the composition of Chen comprises variable regions of <u>a</u> <u>single immunoglobulin</u>, the 38C13 Id. See, *e.g.*, 4776, first sentence of column 1: ". . . we have shown that a fusion between *the* 38C13 tumor Id and GM CSF converts *the* tumor Id into a strong immunogen . . " (*emphasis added*). Chen further makes clear that the antibody-cytokine fusion disclosed consists of heavy and light chain variable regions of <u>only</u> the 38C13 Id immunoglobulin, stating that "the resulting [chimeric Id] protein is composed of *the* 38C13 heavy chain variable region (V_H38C) and *the* light chain variable region ($V\kappa 38C$) fused to the human IgG1 heavy chain constant region ($C\gamma 1$) and κ light chain constant region ($C\kappa$), respectively" (Chen, p4777, column 1, emphasis added).

<u>B. Chen does **not** disclose expression of at least three different variable regions.</u>

As noted above, a single immunoglobulin has only two different variable regions. Chen provides variable regions from only *a single immunoglobulin*. Specifically, Chen discloses one type of V_H region, *i.e.*, the V_H38C region (and thus does <u>not</u> provide at least two <u>different</u> V_H regions). Similarly, Chen discloses only one type of V_L region, $V\kappa 38C$ (and thus does <u>not</u> provide at least two <u>different</u> V_L regions"). Chen thus discloses the

expression of <u>only two different variable regions</u>.

The fact that the V_H and V_L regions of Chen may differ from each other by one or more idiotopes is irrelevant to the present claims. At indicated in each of Claims 25, 28 and 29, the claimed compositions contain at least two V_H regions that differ <u>from each other</u> by at least one idiotope, and/or at least two V_L regions that differ <u>from each other</u> by at least one idiotope. A composition having idiotope differences only between V_H and V_L regions does not provide these claim elements.

Claims 25-29 are not anticipated

As previously noted, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP 2131, citing *Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d. 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)*.

The present claims recite the expression of at least **three** <u>different</u> variable regions of immunoglobulin molecules. Chen discloses a composition having only two different variable regions and fails to teach or suggest a composition comprising three <u>different</u> variable regions of immunoglobulins. More precisely, Chen does not teach or suggest <u>any</u> of combinations of variable regions expressly required by the claims:
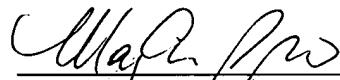
1. one V_H region and at least two <u>different</u> V_L regions (a total of three <u>different</u> variable regions)

2. two <u>different</u> V_H regions and one V_L region, (a total of three different variable regions.

3. two <u>different</u> V_H regions and at least two <u>different</u> V_L regions (a total of four <u>different</u> variable regions.

As such, the Chen reference does <u>not</u> teach each and every element as set forth in Claims 25-29, either expressly or inherently, and thus does not anticipate these claims under 35 U.S.C. § 102(b). Applicant thus respectfully requests that this rejection be removed.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all reasons for rejection should be removed and Applicant's claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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